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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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ALSTON & BIRD LLP
PIONEER HI-BRED INTERNATIONAL, INC.
BANK OF AMERICA PLAZA
101 SOUTH TYRON STREET, SUITE 4000
CHARLOTTE, NC 28280-4000

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| EXAMINER |
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KALLIS, RUSSELL

| ART UNIT | PAPER NUMBER |
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| 1638 | 9 |

DATE MAILED: 06/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | |
|------------------------------|------------------------|---------------------|
| Office Action Summary | Application No. | Applicant(s) |
| | 09/478,567 | RAO ET AL. |
| | Examiner | Art Unit |
| | Russell Kallis | 1638 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 25 March 2003.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-20 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ . | 6) <input type="checkbox"/> Other: _____ . |

DETAILED ACTION

Election/Restrictions

Applicant's traversal of the restriction of Claims 1-20 filed on 2/25/03 is acknowledged.

The restriction is withdrawn and Groups I and II are rejoined.

Claims 1-20 are pending and Claims 1-20 are examined.

Specification

The specification is objected to under 37 CFR 1.821(d) for failing to provide a sequence identifier for each individual sequence. Figures 1, 2, and 4 describe VSP sequences that each must have a sequence identifier. Correction is required.

Claim Rejections - 35 USC § 112

Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant broadly claims an isolated nucleic acid encoding an engineered protein having altered amino acid composition binding to an interacting molecule that binds to the native form of the protein.

Applicant describes the amino acid sequence for VSP β and proposed methionine enriched VSP β variants in Figure 2 and Figure 4; and amino acid sequences SEQ ID NO: 1-10 of unknown function in the sequence listing.

Applicant does not describe any isolated nucleic acid molecules encoding any engineered protein having any altered amino acid composition other than the polynucleotide sequence encoding VSP β -met10 in Figure 4.

Given the claim breadth and lack of guidance as discussed above, the specification does not provide an adequate written description of the claimed invention.

See *University of California V. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

The court also addressed the manner by which genus of cDNAs might be described: “A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.” *Id.* At 1406.

Based upon the disclosure of a VSP β -met10 (Figure 4), there is insufficient relevant identifying characteristics to allow one skilled in the art to completely determine the structure of nucleic acid molecule altered to introduce changes into the encoded amino acid sequence, other than VSP β -met10 (Figure 4), that increase the essential amino acid composition, including mutants and allelic variants, absent further guidance. Since the claimed genus encompasses undisclosed or yet to be discovered sequences that increase the essential amino acid composition, the disclosure of VSP β -met10 (Figure 4) does not provide adequate description of the claimed

genus. In view of the level of knowledge and skill in the art one skilled in the art would not recognize from Applicant's disclosure that Applicant was in possession nucleic acid molecules encoding proteins that have an increase in the essential amino acid composition, other than VSP β -met10 (Figure 4), that increase the level of essential amino acids as broadly claimed (see Written Description Requirement published in Federal Register/Vol.66, No. 4/ Friday, January 5, 2001/Notices; p. 1099-1111).

Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant broadly claims an isolated nucleic acid encoding an engineered protein having altered amino acid composition that binds to an interacting molecule that binds to the native form of the protein and plants transformed therewith.

Applicant teaches proposed methionine enriched VSP β variants based on conserved amino acid residues within VSP homologues (pages 15-16 and Figure 2); positions of possible tolerated amino acid substitutions within VSP β (pages 16-19); a strategy for isolating correctly folded methionine enriched variants of VSP β by testing for binding to a VSP β specific antibody (pages 19-22) and methionine enriched variant VSP β -10 binding to wild type VSP β specific antibodies (page 19).

Applicant does not teach plants transformed with an isolated nucleic acid encoding an engineered protein having altered amino acid composition binding to an interacting molecule that binds to the native form of the protein other than variant VSP β -10.

Interacting molecules do not predictably interact with proteins. Bendayan S. *et al.* teach a Mab raised against one antigen cross-reacting with determinants from other proteins (Bendayan S. *et al.* The Journal of Histochemistry and Cytochemistry, 1995; Vol. 43, No. 9; pp. 881-886 see abstract column 1 lines 9-14 and page 882 column 2 to page 883 column 1). Further, it is well known in the art that Mab recognize linear portions of a protein of up to 8 contiguous amino acids and thus, would not necessarily discriminate against non-native or non-corresponding VSP β variants.

Given the unpredictability in the art as to which substitutions to an isolated nucleic acid that would be tolerated; the breadth of the claims encompassing a nucleic acid encoding a protein altered in some unspecified way in the amount of an essential amino acid; the lack of guidance in the examples of the specification or in the prior art as to which substitutions would best serve the invention and increase the essential amino acid content of protein encoded by a polynucleotide used to transform a plant; although one of skill in the art can readily make nucleotide substitutions to a polynucleotide sequence one would not know based upon Applicant's disclosure which embodiments would be inoperable and predictably eliminated, and thus undue trial and error experimentation would be needed by one skilled in the art to make, clone, and express a multitude of non-exemplified variants of an isolated nucleic acid and test for a protein, altered in an unspecified way, that interacted with a molecule that interacted with a native form of the protein and would require one of skill in the art to test in a myriad of non-exemplified plants for expression. Therefore, the invention is not enabled.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because “the said protein” of line 3 is already engineered. The claim recites “altered amino acid composition” as a property of the engineered protein. The claim then recites “wherein said amino acid composition has been altered by introducing amino acid changes into said protein”. The claim is apparently referencing two different proteins.

At Claim 1, line 4, “interacting molecule” is indefinite. It is not clear if all possible molecular interactions are included the limitation or only specific interactions with specific molecules.

At Claim 1, line 4, “capable of binding” is indefinite. It is unclear if the binding is specific or non-specific or under what conditions binding would occur. It is suggested that “capable of” be deleted.

At Claim 1, line 4, “a corresponding native protein” is indefinite. “Corresponding” does not adequately define the relationship between the two proteins. It is unclear if the two proteins correspond because they bind the same molecule or because of some other relationship between the two. It is unclear which binds to the native protein, the engineered protein or the interacting molecule.

At Claim 2, there is no comparative basis for “wherein said amino acid changes increase the levels of at least one essential amino acid in the protein”.

At Claim 2, and throughout the claims, “essential amino acid” is indefinite.

At Claim 2, “the protein” is indefinite. It is unclear which protein is referenced.

Claims 2-7, recite the limitation "the nucleotide sequence" in line 1. There is insufficient antecedent basis for this limitation in the claims.

At Claim 3, line 1, "the nucleotide sequence encoding" is either grammatically incorrect or an object is missing after "encoding".

At Claim 4, line 1, "wherein said is vegetative storage protein" is missing a subject and therefore is grammatically incorrect.

At Claim 4, line 1, "vegetative storage protein" is missing an article.

At Claim 8, "gene" is indefinite. "Gene" encompasses regulatory elements, coding, and non-coding regions. It appears this is not Applicant's intention. If appropriate, the term "polynucleotide" can be used to denote nucleic acid molecules that encode a polypeptide. All subsequent recitations of "gene" are also rejected.

At Claim 8, line 3, "an interacting molecule" is indefinite. It is not clear if all possible molecular interactions are included the limitation or only specific interactions with specific molecules.

At Claim 8, line 4, "corresponding native protein" is indefinite. "Corresponding" does not adequately define the relationship between the two proteins. It is unclear if the two proteins correspond because they bind the same molecule or because of some other relationship between the two.

Claims 8, recites the limitation "wherein said protein" in lines 2-3. There is insufficient antecedent basis for this limitation in the claims.

At Claims 9, 11, and 12, there is no comparative basis for the increases.

At Claims 9, 11, 12 and 13, there is no comparative basis for "the protein".

Claims 9, 11, and 12 recite the limitation "the protein" in line 2. There is insufficient antecedent basis for this limitation in the claim.

At Claim 12, "are" should be changed to --is--.

At Claim 13, "vegetative storage protein" requires an article.

Claim 17 recites the limitation "wherein said dicot" in line 1. There is insufficient antecedent basis for this limitation in the claim.

At Claims 18-20, "Seed" requires an article.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 18-20 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The seeds of Claims 18-20 encompass untransformed seeds, which are a product of nature and not one of the five classes of patentable subject matter. Due to Mendelian inheritance of genes, a single gene introduced into a parent plant would only be transferred at most to half the male gametes and half the female gametes. This translates into only two thirds of the progeny or seeds having at least a single copy of the transgene and one quarter of the progeny or seeds would not carry a copy of the transgene. Since the claims encompass seeds that lack the transgene, the claims encompass seeds that are indistinguishable from plants and seeds that would occur in nature.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-14, 17, and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Jung R. *et al.* WO 97/35023 published September 25, 1997.

The claims are indefinite as discussed *supra*, and thus read on any transgenic plant transformed with any polynucleotide altered to encode a protein having amino acid changes, and that interacts with any molecule, in any fashion, as does the corresponding native protein.

The claims are broadly drawn to soybean plants transformed with a nucleic acid molecule encoding a vegetative storage protein engineered to have at least one essential amino acid increased to 10% of total amino acid content compared to the native protein wherein the engineered protein binds to a molecule that binds to the native form of the protein.

Jung teaches an isolated soybean 2S Albumin protein cDNA (Example 2 page 32); an isolated soybean 2S Albumin protein cDNA engineered (Albumin 1/3) to have 13.14% lysine and 12.4% methionine and cysteine (Example 3 pages 35-36); transformation of soybean plants transformed with cDNA encoding modified soybean 2S Albumin, a vegetative seed protein, said engineered peptides and seeds thereof (Example 4 pages 37-42); and preparation of Albumin specific antibodies that bind to both native and engineered soybean 2S Albumin proteins (Example 4 pages 42-43). Thus, the reference teaches all the limitations of Claims 1-14, 17, and 18.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Tarczynski M. *et al.* U.S. Patent 6,080,913 filed September 25, 1996.

The claims are indefinite as discussed supra, and thus read on any transgenic plant transformed with any polynucleotide altered to encode a protein having amino acid changes, and that interacts with any molecule, in any fashion, as does the corresponding native protein.

The claims are drawn to maize and soybean plants transformed with a nucleic acid molecule encoding a vegetative storage protein engineered to have at least one essential amino acid increased to 10% of total amino acid content compared to the native protein wherein the engineered protein binds to a molecule that binds to the native form of the protein.

Tarczynski teaches transformation of maize with an engineered cDNA from barley encoding a high lysine derivative of alpha-hordothione, a seed vegetative storage protein, targeted to the seed (Example III columns 13-14); and an endoplasmic reticulum targeting sequence KDEL for retention in the ER of maize that interacts with the molecules of the ER as do the corresponding native maize proteins. Thus the reference teaches all the limitations of Claims 1-10, 13, 15-16 and 18-20.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jung R. *et al.* WO 97/35023 published September 25, 1997 in view of Gordon-Kamm *et al.* *The Plant Cell*, July 1990; Vol. 2; pp. 603-608.

The claims are drawn to soybean and maize plants transformed with a nucleic acid molecule encoding a vegetative storage protein engineered to have an essential amino acid increased to 10% of total protein amino acid content compared to the native protein wherein the engineered protein binds to a molecule that binds to the native form of the protein.

The teachings of Jung are discussed supra.

Jung does not teach Maize transformation.

Gordon-Kamm *et al.* teach transformation of maize (pages 615-616).

It would have been obvious at the time of Applicant's invention to modify the invention of Jung to include a method for transformation of maize. One of skill in the art would have been motivated by the knowledge common in the art that the method of maize transformation as taught by Gordon-Kamm *et al.* is valuable for genetic engineering of plants to enhance the amino acid profile of a plant by expression of an engineered protein as taught by Jung *et al.* are and given the success of Gordon-Kamm in the expression of exogenous genes in Maize and Jung in expression of amino acid enhanced peptides in soybean, one would have had a reasonable

expectation of success of expressing genes encoding amino acid enhanced peptides in transformed maize plants and plant cells.

Art Unit: 1638

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (703) 305-5417. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Russell Kallis Ph.D.
June 14, 2003

Phuong Bui
PHUONG T. BUI
PRIMARY EXAMINER
6/16/03